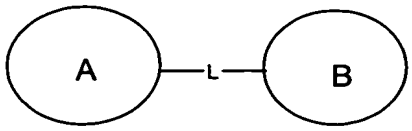
CLAIMS

1. The use of a compound of formula (Ia):



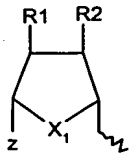
(Ia)

wherein A and B are independently selected from a cyclic ring, wherein each of which cyclic rings A and B may be optionally substituted at at least one ring position; and
L is a suitable linker;
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in inhibiting ADP-ribosyl cyclase.

2. The use according to claim 1 wherein one or more of the cyclic rings A and B is a heterocyclic ring.

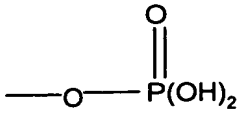
3. The use according to claim 1 or 2 wherein one or more of the cyclic rings A and B is a five membered ring.

4. The use according to any one of claims 1-3 wherein cyclic ring A has the formula (II):



(II)

wherein X_1 is independently selected from O, S, CH_2 or a halo derivative thereof;
each of R_1 or R_2 is a substituent group independently selected from OH, OR, SH, SR, halo (preferably F), NH_2, NHR or

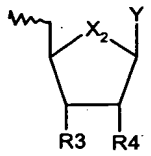


and wherein R is independently a hydrocarbyl group, preferably a C_{1-12}, preferably C_{1-6}, alkyl or acyl group (which may be optionally substituted), and
Z is a hydrocarbyl.

5. The use according to claim 4 wherein X_1 is O.

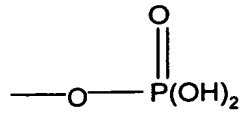
6. The use according to claim 4 wherein each of R_1 or R_2 is OH.

7. The use according to any one of the preceding claims wherein cyclic ring B has the formula (III):



(III)

wherein X_2 is independently selected from O, S, CH_2 or a halo derivative thereof;
each of R_3 or R_4 is a substituent group independently selected from OH, OR, SH, SR, halo (preferably F), NH_2, NHR or



and wherein R is independently a hydrocarbyl group, preferably a C_{1-12}, preferably C_{1-6}, alkyl or acyl group (which may be optionally substituted); and
Y is a hydrocarbyl.

8. The use according to claim 7 wherein X_2 is O.

9. The use according to claim 7 wherein each of R_3 or R_4 is an OH.

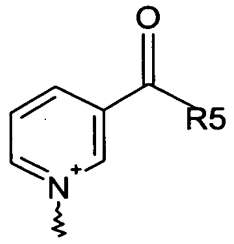
10. The use according to any one of claims 4-9 wherein each of Y or Z is independently selected from an aromatic group or a substituted aromatic group

11. The use according to any one of claims 4-10 wherein each of Y or Z is independently selected from a heteroaromatic group or a substituted heteroaromatic group.

12. The use according to claim 11 wherein the heteroaromatic group or the substituted heteroaromatic group comprises a purine or a substituted purine structure.

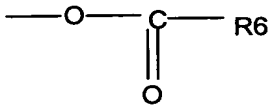
13. The use according to claims 4-6 or to claims 10-12 when dependent upon claims 4-6 wherein Z is a pyridine or a substituted pyridine.

14. The use according to claims 4-6 or to claims 10-12 when dependent upon claims 4-6 wherein Z has the formula (IV):



(IV)

wherein R_5 is NH_2, OH or

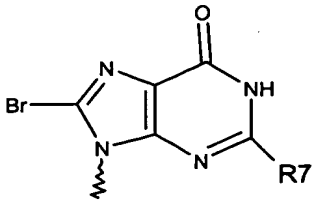


wherein R_6 is a hydrocarbyl group, preferably C_{1-12}, preferably C_{1-6}, alkyl or acyl group (which may be optionally substituted).

15. The use according to claims 7-12 wherein Y is a purine or a substitute purine.

16. The use according to claims 7-12 wherein Y comprises two fused heterocyclic rings, wherein each of said heterocyclic rings independently comprises nitrogen and carbon atoms in their respective rings, and wherein each of said heterocyclic rings may be optionally substituted at at least one ring position.

17. The use according to claim 16 wherein Y has the formula (V):

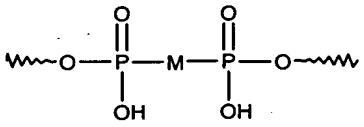


(V)

wherein R_7 is independently H or NH_2.

18. The use according to any one of the preceding claim wherein said linker is non-hydrolysable.

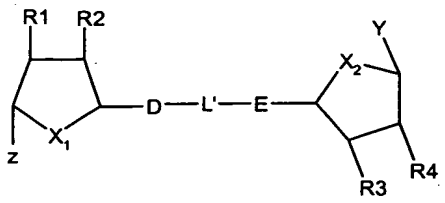
19. The use according to any one of the preceding claims wherein the linker has the formula (VI):



(VI)

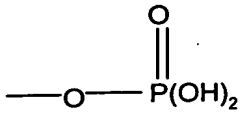
wherein M is independently selected from O, NH, CH_2 or a halo derivative thereof.

20. The use according to any one of the preceding claims wherein said compound is a compound of formulae (Ib):



(Ib)

wherein D and E are independently selected from O, S, CH_2 or a halo derivative thereof;
wherein each of X_1 and X_2 is independently selected from O, S, CH_2 or a halo derivative thereof;
each of R_1, R_2, R_3 or R_4 is a substituent group independently selected from OH, OR, SH, SR, halo (preferably F), NH_2, NHR or



and wherein R is independently a hydrocarbyl group, preferably a C_{1-12}, preferably C_{1-6}, alkyl or acyl group (which may be optionally substituted);

each of Z and Y is a hydrocarbyl; and

L' is the remainder of linker L;

or a pharmaceutically acceptable salt thereof.

21. The use of a compound according to any one of the preceding claims wherein said compound is one or more of a nicotinamide adenine dinucleotide analogue or a nicotinic acid adenine dinucleotide phosphate analogue.

22. The use of a compound according to any one of the preceding claims wherein said compound is one or more of: nicotinamide 8-bromohypoxanthine dinucleotide; nicotinamide 7-deazahypoxanthine dinucleotide; nicotinamide hypoxanthine dinucleotide; nicotinamide 6-thiohypoxanthine dinucleotide; nicotinamide 8-bromoguanine dinucleotide.

23. The use of a compound according to any one of preceding claims wherein said medicament is for use in modulating the immune response of a mammal.

24. The use of a compound according to any one of the preceding claims wherein said medicament is for use in treating an autoimmune disease or a graft rejection.

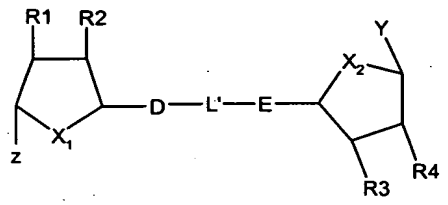
25. The use of a compound according to claim 24 wherein the autoimmune disease is selected from thyroiditis, insulitis, multiple sclerosis, iridocyclitis, uveitis, orchitis, hepatitis, Addison's disease, myasthenia gravis, rheumatoid arthritis and lupus erythematosus.

26. The use of a compound according to any one of the preceding claims wherein said medicament is for use in treating or preventing an immune disorder in a human or animal.

27. A pharmaceutical composition comprising a compound as defined in any one of the preceding claims or a pharmaceutically acceptable salt thereof admixed with a pharmaceutically acceptable carrier, diluent or excipient.

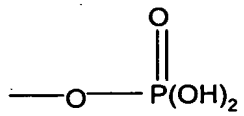
28. A pharmaceutical composition according to claim 27 wherein said composition comprises one or more additional pharmaceutically active compounds.

29. A compound of formula (Ib):



(Ib)

wherein D and E are independently selected from O, S, CH_2 or a halo derivative thereof;
wherein each of X_1 and X_2 is independently selected from O, S, CH_2 or a halo derivative thereof;
each of R_1, R_2, R_3 or R_4 is a substituent group independently selected from OH, OR, SH, SR, halo (preferably F), NH_2, NHR or



and wherein R is independently a hydrocarbyl group, preferably a C_{1-12}, preferably C_{1-6}, alkyl or acyl group (which may be optionally substituted);
each of Z and Y is a hydrocarbyl; and
L' is the remainder of linker L.

30. A compound according to claim 29 wherein each of X_1 and X_2 is O.

31. A compound according to claims 29 or 30 wherein each of R_1, R_2, R_3 or R_4 is an OH.

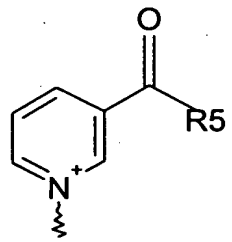
32. A compound according to claims 29-31 wherein each of Y or Z is independently selected from an aromatic group or a substituted aromatic group

33. A compound according to claims 29-32 wherein each of Y or Z is independently selected from a heteroaromatic group or a substituted heteroaromatic group.

34. A compound according to claims 29-33 wherein the heteroaromatic group or the substituted heteroaromatic group comprises a purine or a substituted purine structure.

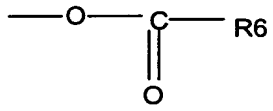
35. A compound according to claims 29-34 wherein Z is a pyridine or a substituted pyridine.

36. A compound according to claims 29-34 wherein Z has the formula (IV):



(IV)

wherein R_5 is NH_2, OH or

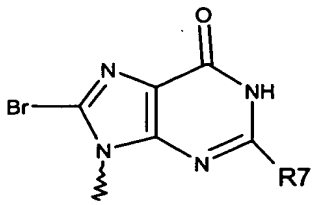


wherein R_6 is a hydrocarbyl group, preferably C_{1-12}, preferably C_{1-6}, alkyl or acyl group (which may be optionally substituted).

37. A compound according to claims 29-36 wherein Y is a purine or a substituted purine.

38. A compound according to claims 29-36 wherein Y comprises two fused heterocyclic rings, wherein each of said heterocyclic rings independently comprises nitrogen and carbon atoms in their respective rings, and wherein each of said heterocyclic rings may be optionally substituted at at least one ring position.

39. A compound according to claims 29-36 wherein Y has the formula (V):

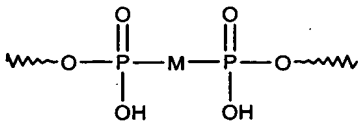


(V)

wherein R_7 is independently H or NH_2.

40. A compound according to any one of claims 29-39 wherein said linker is non-hydrolysable.

41. A compound according to any one of claims 29-40 wherein the linker has the formula (VI):



(VI)

wherein M is independently selected from O, NH, CH_2 or a halo derivative thereof.

42. A compound according to any one of claims 29-41 wherein said compound is a nicotinamide adenine dinucleotide analogue.

43. A compound according to any one of claims 29-42 wherein said compound is one or more of: 8-bromo-nicotinamide hypoxanthine dinucleotide; 7-deaza-nicotinamide hypoxanthine dinucleotide; nicotinamide hypoxanthine dinucleotide; 6-thio-nicotinamide hypoxanthine dinucleotide.

44. A compound according to any one of claims 29-43 for use as a medicament.

45. Use of a compound according to any one of claims 29-44 in the manufacture of a medicament for use in inhibiting ADP-ribosyl cyclase.

46. A medicament comprising a compound according to any one of claims 29-45.

47. A method of inhibiting ADP-ribosyl cyclase comprising the step of contacting an ADP-ribosyl cyclase with a compound defined in any of claims 1-26 or 29-46 or a composition according to claims 27 or 28.

48. A method of modulating the concentration of cADPR and/or NAADP+ in a cell comprising the step of contacting an ADP-ribosyl cyclase with a compound defined in any of claims 1-26 or 29-46 or a composition according to claims 27 or 28.

49. A method according to claim 48 wherein the concentration of cADPR is decreased.

50. A method according to claims 48 wherein the concentration of NAADP+ is decreased to below an activating concentration, such as to a concentration less than or equal to 10 nM.

51. A method according to claims 48 wherein the concentration of NAADP+ is increased to an inactivating concentration, such as to a concentration greater than or equal to 10 μM.

52. A method of modulating intracellular Ca^{2+} levels in a T-cell comprising the step of contacting an ADP-ribosyl cyclase with a compound defined in any of claims 1-26 or 29-46 or a composition according to claims 27 or 28.

53. A method of modulating T cell activity, which comprises the step of contacting an ADP-ribosyl cyclase with a compound defined in any of claims 1-26 or 29-46 or a composition according to claims 27 or 28.

50. A method according to any one of claims 43-49 wherein said step is carried out *in vitro*.

51. A method according to any one of claims 43-49 wherein said step is carried out *in vivo*.

52. A method of treating or preventing a disease in a human or animal patient which method comprises administering to the patient an effective amount of a compound as defined in any one claims 1-24 or 27-40 or a composition according to claims 25 or 26.

53. A pharmaceutical pack comprising one or more compartments, wherein at least one compartment comprises one or more of the compounds defined in any of claims 1-24 or 27-40 or a composition according to claims 25 or 26.

54. A process of preparation of a pharmaceutical composition according to claims 25 or 26, said process comprising admixing one or more of the compounds defined in any of claims 1-24 or 27-40 with a pharmaceutically acceptable diluent, excipient or carrier.

55. An assay method for identifying an agent that can directly or indirectly inhibit ADP-ribosyl cyclase in order to treat an autoimmune disease or a graft rejection, the assay method comprising: contacting an agent with ADP-ribosyl cyclase; and measuring the activity of ADP-ribosyl cyclase; wherein a downregulation of activity of ADP-ribosyl cyclase in the presence of the agent is indicative that the agent may be useful in the treatment of an autoimmune disease or a graft rejection.

56. A process comprising the steps of:

(a) performing the assay according to claim 55;

(b) identifying one or more agents that can directly or indirectly downregulate the activity of ADP-ribosyl cyclase; and

(c) preparing a quantity of those one or more identified agents.

57. A method of treating an autoimmune disease or graft rejection, by downregulating the activity of ADP-ribosyl cyclase *in vivo* with an agent; wherein the agent is capable of directly or indirectly downregulating the activity of ADP-ribosyl cyclase in an *in vitro* assay method; wherein the *in vitro* assay method is the assay method defined in claim 55.

58. Use of an agent in the preparation of a pharmaceutical composition for the treatment of an autoimmune response or a graft rejection, wherein the agent is capable of directly or indirectly downregulating the activity of ADP-ribosyl cyclase when assayed *in vitro* by the assay method according to claim 55.

59. An agent identified by the assay method according to claim 55.

60. An agent according to claim 59 for use in medicine.

61. An agent according to claim 60 for use in treating an autoimmune disease or a graft rejection.

62. Use of one or more compounds defined in any of claims 1-24 or 27-40 in an assay for identifying candidate compounds that are capable of influencing the activity of ADP-ribosyl cyclase.